



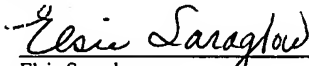
PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application of: Kevin R. Stone et al.
Serial No.: 10/665,844
Filing Date: September 19, 2003
Title: Anterior Cruciate Ligament Xenographs
Docket: CROL-0114CP2CN3

CERTIFICATE OF EXPRESS MAILING

I hereby certify that this correspondence is being deposited with the United States Postal Service as "Express Mail Post Office to Addressee," Express Mail Label No. EY 961806276 US in an envelope addressed to MS: Petition, Commissioner for Patents, PO Box 1450, Alexandria, VA 22313-1450, on October 19, 2006.


Elsie Saraglow

MS: Petition
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

PETITION TO REVIVE

Dear Sir:

Applicants hereby petition for withdrawal of the Notice of Abandonment for the above-captioned application.

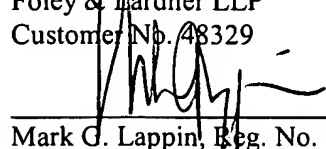
Applicants received a Notice of Abandonment, mailed September 19, 2006, indicating the above-captioned application was abandoned because of failure to respond to the Office Action mailed on January 17, 2006.

Applicants submitted a Response to Office Action on July 17, 2006. Attached herewith is a copy of the Transmittal Letter, Response to Office Action, Exhibit A, Exhibit B, Petition for Three-Month Extension of Time, U.S. Patent and Trademark date-stamped postcard receipt, and date-stamped Express Mail Label, indicating these items were timely filed on July 17, 2006.

In view of the foregoing, Applicants respectfully request withdrawal of abandonment.

Although Applicants do not believe a fee is due with the filing of this paper, the Commissioner is hereby authorized to charge any fees that may be required, or credit any overpayment, to Deposit Account No. 50-3431. A duplicate of this sheet is enclosed.

Respectfully submitted,
Foley & Dardner LLP
Customer No. 48329


Mark G. Lappin, Reg. No. 26,618

Date: October 19, 2006

111 Huntington Avenue
Boston, MA 02199
Telephone: (617) 342-4000; Fax: (617) 343-4001



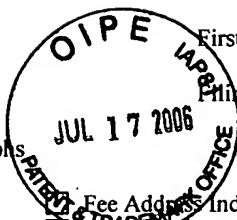
Express Mail No. EV 426288090 US

Date Mailed: July 17, 2006

Serial No.: 10/665,844

Inventor: Kevin R. Stone, et al.

Title: Anterior Cruciate Ligament Xenographs



First Class Mail ☐

Filing Date: 09/19/2003

- | | |
|---|--|
| <input type="checkbox"/> Affidavit/Declaration | <input type="checkbox"/> Fee Address Indication Form |
| <input checked="" type="checkbox"/> Response (5 Pages) | <input type="checkbox"/> Fee Calculation |
| <input type="checkbox"/> Application; _____ Pages | <input type="checkbox"/> Issue Fee Transmittal |
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| <input type="checkbox"/> Appeal, Notice of | <input type="checkbox"/> Response to Not. to File Missing Parts |
| <input type="checkbox"/> Assignment with recordation cover sheet | <input checked="" type="checkbox"/> Petition for Extension of Time (1 page)
(in duplicate) (3 months) |
| <input type="checkbox"/> Brief (in triplicate) | <input type="checkbox"/> Pet. Under 37 C.F.R. _____ |
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Address Change |
| <input type="checkbox"/> Design Application | <input type="checkbox"/> Sequence Listing w/Computer |
| <input type="checkbox"/> Disclaimer | <input checked="" type="checkbox"/> Return Postal Card |
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| <input type="checkbox"/> w/refs. <input type="checkbox"/> w/o refs. | <input type="checkbox"/> Status Letter |
| <input type="checkbox"/> Drawings | <input checked="" type="checkbox"/> Transmittal Letter (duplicate) |
| ____ Sheets _____ Figures | |

Other: Exhibits A and Exhibit B

CROL-114CP2CN3 (91957-010205)

BY: MGL

GT-806

DUE DATE: _____

DEADLINE: _____

DOCKETED: 7/24/06

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PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Kevin R. Stone et al.
Serial No.: 10/665,844
Filing Date: September 19, 2003
Title: Anterior Cruciate Ligament Xenographs
Docket: CROL-0114CP2CN3 (91957-010205)

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Ben Joplin

MS: Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

TRANSMITTAL LETTER

Dear Sir:

Enclosed herewith for filing in connection with the above-identified patent application are the following:

1. Response to Office Action (5 pages);
2. Exhibit A (2 pages);
3. Exhibit B (2 pages)
4. Petition for Three-Month Extension of Time (1 page) (in duplicate); and
5. Return Postcard.

The Commissioner is hereby authorized to charge \$510.00 for Three-Month Extension of Time fee, and any additional fees which may be required, or credit any overpayment, to Deposit Account No. 50-2678. A duplicate of this sheet is enclosed.

Respectfully submitted,
Greenberg Traurig, LLP
Customer No. 35893

Date: July 17, 2006

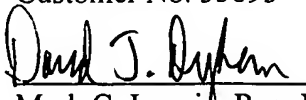
 Reg. No. 46,678 for
Mark G. Lappin, Reg. No. 28,618
One International Place
Boston, MA 02110
Telephone: (617) 310-6010, Fax: (617) 310-6001



EXHIBIT A

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1: [Transplantation](#). 1995 Oct 27;60(8):841-7.

[Related Articles, Links](#)

Enzymatic removal of alpha-galactosyl epitopes from porcine endothelial cells diminishes the cytotoxic effect of natural antibodies.

[LaVecchio JA](#), [Dunne AD](#), [Edge AS](#).

Department of Molecular and Cellular Biology, Diacrin Inc., Charlestown, Massachusetts 02129, USA.

Xenotransplantation of tissues between discordant species such as pig into human is not yet feasible due to the problem of hyperacute rejection. This rapid response to xenogeneic tissue is mediated by natural antibodies that react with antigens on the xenograft. A number of xenoantigens consist of carbohydrate residues, and a terminal galactose in alpha linkage has been shown to be involved in hyperacute rejection of pig-to-human xenografts. We show that alpha-linked galactose on porcine endothelial cells is a major epitope recognized by IgG and IgM antibodies present in monkey and human sera. Endothelial cells that had been treated with alpha-galactosidase did not react with fluorescein-labeled Griffonia simplicifolia I B4 (GS-IB4), a lectin that detects the alpha-galactosyl epitope on intact cells. The reactivity of both human and cynomolgus monkey serum with endothelial cells was decreased by 59% to 90% after treatment with coffee bean alpha-galactosidase. Using a colorimetric assay for cell viability, we show that natural antibodies present in the sera of cynomolgus monkey and humans are cytotoxic to porcine endothelial cells in the presence of exogenously added complement. When the terminal alpha-galactosyl residues were removed by enzymatic digestion, the cytotoxic effect of natural antibodies on porcine endothelial cells was diminished by > 80%. Evaluation of the time course of reappearance of the alpha-galactosyl epitope at the cell surface revealed that 48 hr after alpha-galactosidase treatment, binding of GS-IB4 was diminished by 60%. These results suggest that glycosidase treatment of cells to be transplanted could prevent hyperacute rejection mediated by natural antibodies.

PMID: 7482745 [PubMed - indexed for MEDLINE]

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EXHIBIT B



Subst. Form PTO-1449 INFORMATION DISCLOSURE CITATION IN AN APPLICATION (Use several sheets if necessary)	Docket Number (Optional) CROL-114CP2CN	Application Number To be assigned
	Kevin R. Stone et al	
	April 2, 2001	

U. S. Patent Documents						
EXAMINER INITIAL	DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE
	5,007,934	4/91	Stone			
	5,067,962	11/91	Campbell et al.			
	5,071,741	12/91	Brockbank			
	5,078,744	1/92	Chvapil			
	5,092,894	3/92	Kenny			
	5,116,374	5/92	Stone			
	5,131,850	7/92	Brockbank			
	5,158,574	10/92	Stone			
	5,160,313	11/92	Carpenter et al.			
	5,171,273	12/92	Silver et al.			
	5,171,322	12/92	Kenny			
	5,171,660	12/92	Carpenter et al.			
	5,192,312	3/93	Orton			
	5,216,126	6/93	Cox et al.			
	5,306,304	4/94	Gendler			
	5,306,311	4/94	Stone et al.			

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

	Rubak et al., <i>Acta Orthop. Scand</i> , 53:181-186 (1982).
	Engkvist, Ove, <i>Scand. J. Plast. Reconstr. Surg.</i> , 13:361-369 (1982).
	Collins et al., Xenotransplantation, Characterization of Porcine Endothelial Cell Determinants Recognized by Human Natural Antibodies, 1:36-46 (1994).
	Satake et al., Xenotransplantation, Limited Specificity of Xenoantibodies In Diabetic Patients Transplanted With Fetal Porcine Islet Cell Clusters. Main Antibody Reactivity Against α -linked Galactose-Containing Epitopes, 1:89-101 (1994).
	LaVecchio et al., Transplantation, Enzymatic Removal of Alpha-Galactosyl Epitopes From Porcine Endothelial Cells Diminishes The Cytotoxic Effect of Natural Antibodies, 60:841-847. (1995)

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP § 609; Draw line through citation if not in conformance and not considered. Include copy with next communication to applicant.



PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Kevin R. Stone et al.
Serial No.: 10/665,844
Filed: September 19, 2003
Title: Anterior Cruciate Ligament Xenographs
Examiner: Saucier, Sandra E. Art Unit: 1651
Atty: Docket: CROL-0114CP2CN3 (91957-010205)

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Ben Joplin

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Alexandria, VA 22313-1450

REQUEST FOR THREE-MONTH EXTENSION OF TIME

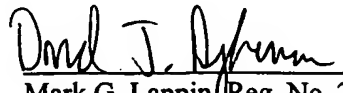
Sir:

Pursuant to 37 C.F.R. 1.136(a)(3), applicants hereby petition for a three-month extension of time to respond to the Office Action dated January 17, 2006, in the above-identified application. With the extension, the response is due up to, and including, July 17, 2006. Please charge the fee of \$510.00 based on small entity status, in payment of the fee required by 37 C.F.R. 1.17(a)(3), to our Deposit Account No. 50-2678.

Please charge any fees that may be due, or credit any overpayment of same, to Deposit Account No. 50-2678. A duplicate of this sheet is enclosed.

Respectfully submitted,
Greenberg Traurig, LLP
Customer No. 35893

Date: July 17, 2006

 Reg. No. 46,678
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Facsimile: (617) 310-6001